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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,790	03/22/2001	Keith D. Allen	R-855	5557

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/816,790	ALLEN ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-43,49,50 and 52-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-43,49,50 and 52-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 40-43, 49, 50, 52-57 are pending in the application.

This Office Action is in response to the Amendment filed on 8/11/05.

Response to Amendment

The rejection of claim 40 under 35 U.S.C.112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 40-43, 49, 50, 52-57 under 35 U.S.C. 112 1st paragraph (written description) has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 40-43, 49, 50, 52-57 under 35 U.S.C. 101/112 1st paragraph is maintained for reasons set forth of the record mailed on 4/27/05 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 101

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 40-43, 49, 50, 52-57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

In response to this rejection, Applicant presents the same argument as the ones in the response filed on 2/11/05. Further, Applicant asserts that studying the function of the mSTp1 is a substantial utility because there is no further research required to confirm the utility of the claimed mouse in determining mSTp1 function because 1) the value of the knockout mouse is

well established in the art; 2) further characterization of the mouse itself is not required to confirm its utility in studying the mSTp1 function; 3) Applicant has provided an *in vivo* model for studying the function of the mSTp1 gene which is associated with anxiety. Applicant indicates that the claimed invention is purchased by two large pharmaceutical company and database comprising tests of the mouse has been subscribed by three pharmaceutical companies, thus such commercial acceptance more than satisfied the practical utility requirement of 101 and 112 1st paragraph according to *Brenner v. Manson* and *Phillips Petroleum Co. v. U.S. Steel Corp.*, and Lipscomb's Walker on Patents 5:17, p 562 (utility may be evidenced by sales and commercial demand). Applicant further argue that the claimed mouse has phenotypes which do not exhibit perinatal lethality, thus provide more than a clue to a pathway. Moreover, Applicants assert that the utility to study mSTp1 gene function and expression using the claimed mouse is specific to the mSTp1 gene knockout mouse because no other mouse can be used for this purpose. Applicant also gives an example of the functional relationship between Gene X and skin pigmentation, and argue that illustration of the entire pathway is not necessary to establish a patentable utility for the claimed mouse. Applicant further asserts that Olsen does not support the position that knockout mouse have no utility, but rather demonstrate that GABA plays a major role in brain development. Furthermore, Applicant asserts that a mouse exhibiting aggressive behavior and hyperactivity is a valid model for behavioral disorder, and as *In re Brana*, confirmation in human is unnecessary. Applicant alleges that the examiner suggests the aggressive behavior and decreased anxiety is mutually exclusive, and argues the data clearly indicate that the mice can have both phenotypes. Applicant concludes that the mice may be used as a model for anxiety. Lastly, Applicant asserts that the claimed mouse is not limited to its use

as a model for anxiety, but also other developmental pathways as indicated by its phenotype. Applicant thus concludes that the claimed invention has credible, substantial and specific utility which satisfies the statue of 35 U.S.C. 101, and enabled by the instant specification.

These arguments have been fully considered but deemed unpersuasive. The reasons for the utility and non-enablement rejection were discussed in detail in the office action mailed on 4/27/05. In response to Applicant's response regarding any knockout mouse has a well-established utility, the examiner does not agree with Applicant's assertion that the claimed invention has a well-established utility. Applicant is reminded that in MPEP, the guideline for the utility requirement clearly states: "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." In the instant case, the utility that applies to any knockout mouse is not specific to the claimed invention, the mSTp1 transgenic mouse having a null allele. It was well known to knock out a gene to determine its function or what will happen when the gene is not expressed. However, scientific "utility" is not the same as "patentable utility" or a "well-established" utility, of which must be specific, substantial and credible. At the time of filing, knockout mice were used for further research in the art as indicated by the quotations cited by Applicant, for example, studying gene function. However, further research does not rise to the level of a "well-established utility" because such a utility is not substantial. The utility guidelines specifically state that further research is not a "substantial utility." The MPEP states "the following are

examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved..." In the instant case, further study of mice would have been required to determine how to use the mouse of applicant's invention according to the embodiments described in the specification since the overall phenotype of the claimed mice does not correlate with any disorder; Therefore, further study would be required to characterize such association because the teaching of the specification is not sufficient to establish whether the phenotype is directly result from the gene disruption. Further study would be required to determine the function of the disrupted gene and its role in the resultant phenotype. Furthermore, the overall phenotype of the claimed mice does not correlate to any disorder; therefore, further study would be required to determine how to use the mice to study a disorder, screening drugs and treatment for such disorder. Thus, using the mice claimed for further research is not a "substantial utility."

In response to Applicant's argument of the commercial sale of the claimed mouse, Applicant is reminded that the sale of a product does not automatically gives the product patentable use according to the statue of 35 U.S.C.101 and the utility guideline set forth in the MPEP. Commercial success is only considered as secondary evidence for overcoming a 103 (a) rejection according to guidelines set by MPEP. *Brenner v. Manson* does not validate the notion that commercial use automatically gives a claimed product patentable utility. The subscription of three company to the Deltabase does not give automatically gives the claimed mouse

patentable utility because it is unclear what data the companies are interested and what they are used for. The declaration under 37 CFR 1.132 has been fully considered, however, it is not sufficient to provide a patentable utility and enable the instantly claimed invention. The purchase of the claimed mouse by two large pharmaceutical company neither proves commercial success of the claimed mouse nor does it gives the claimed mouse a patentable utility. The case law of *Phillips Petroleum Co. v. U.S. Steel Corp.* 6 USPQ 2d 1065 talks about commercial success in context as secondary consideration in favor of nonobviousness (see page 1096). It states "of course, there must be a nexus "between the merits of the claimed invention and the evidence offered if that evidence is to be given substantial weight enroute to conclusion on the obviousness issue." *Stratoflex* , 713 F.2d at 1539 [218 USPQ at 879] (noting *Solder Removal Co. v. United States Intern. Trade* , 582 F.2d 628, 637 [199 USPQ 129, 137] (C.C.P.A. 1978)). Crystalline polypropylene is one of the most widely used chemical compositions in commerce today. Worldwide demand is presently approximately fourteen billion pounds, with the United States' demand totaling nearly six billion pounds per year. (Mark, Tr. at 503.) 68 Experts from both sides were in general agreement that crystallinity is the characteristic which gives polypropylene its immense commercial value." According to the case law, the commercial success is established by the worldwide use of the claimed compositions and the generation of high revenue from the sale of the claimed composition. However, the sale of the present claimed invention to two pharmaceutical company clear does not mount to such "commercial success." The case law of 9 USPQ 2d 1461 affirmed the earlier case but does not deal with commercial success and practical utility. It states: "correct finding of infringement of otherwise valid claims mandates as a matter of law a finding of utility under §101," however, it does not apply to the

current situation since there is no infringement of the current claimed invention. With regard to the sentence quoted from Lipscomb's Walker on Patents, the examiner cannot comment on it because it is unclear what context such statement was made. For example, what evidence should Applicants provide to establish sales and commercial demand? Is it a secondary evidence to some other requirement? A search of the book reveals that it ends at page 530, there is no page or paragraph 562. As such, this statement alone does not support that sale of this mouse to one company automatically gives the claimed mouse a patentable utility. Therefore, based on the utility requirement set forth in MPEP, the sale of the mouse to one company does not give the claimed mouse a patentable utility.

With regard to the well-established utility of studying gene function as asserted by Applicant, Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). As such, a knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Using the claimed mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype is not specific to the knocked out gene. The examiner

does not agree with Applicant's interpretation of the Olsen reference as teaching knockout mouse has well-established utility, and whether the GABA knockout mouse has well-established utility is beside the point. The relevant issue is whether the claimed mouse having a null mSTp1 gene has patentable utility. The Olsen reference and Crawford reference (cited in earlier office action) both teach that the phenotype of a knockout mouse is unpredictable, and there are instances that the observed phenotype is not directly result from the disruption of a specific gene. In view of such unpredictability in the art, the burden is on Applicant to teach such specific correlation does exist in the specification, and thus the claimed mouse is useful as a disease model. Further, Applicant must teach what specific disease(s) the claimed mouse represents. In the instant case, Applicant fails to do both. As discussed above, the overall phenotype does not correlate to any specific disease. The broad assertion of the claimed mouse can be used to study behavioral disorder is not sufficient to establish as substantial and specific use for the claimed mouse because it is unclear what specific behavioral disorder the mouse is modeling for (ADHD, hyperactivity, hypoactivity?) The examiner is also confused with Applicant's allegation of mutually exclusive behavior such as hyperactivity and decreased anxiety. The examiner's position is simply that the overall phenotype of the claimed mouse is not indicative if said mouse represents any human disease. As for Applicant's assertion of the claimed mouse is useful in other developmental pathway, the specification fails to teach what pathway the mSTp1 gene is involved in and how the claimed mouse can be used as a specific disease model. Furthermore, the example of the relationship of Gene X and skin pigmentation is

irrelevant to the instant claimed invention because the conclusion of such relationship is based on known relationship between X and Y, Y and pigmentation. In the instance of genotypic and phenotypic information of a knockout mouse, whether decreased pigmentation is result from change of X or other factors must be known before a relationship can be established.

In response to Applicant's argument with regard to specific utility, Applicant is again reminded that the asserted utility of the claimed invention need to be credible, substantial and specific according to the 101 statue. The utility of studying mSTp1 function using the claimed mouse fails to meet this requirement (see reasons given above). As discussed in Crawley et al. (page 108 2nd col., 3rd paragraph), no single behavior commonly measured in the open field reflects only anxiety or emotional reactivity. The open field parameters reflects multiple underlying traits which indicates that genes linked to open field performance may be involved in the regulation of many activities including locomotor, exploratory, olfaction and vision. Thus, further research is required to determine which functional pathway the mSTp1 is involved in. There is no support that from the instant specification that said mSTp1 is directly involved in hyperactivity. Moreover, if the phenotype of the mouse is not directly resulted from the disruption of the gene, the association between the phenotype is not specific to the disruption of the mSTp1 gene. As such, the claimed mouse fails to meet the standard.

For reasons given in the previous office action and above, the specification fails to disclose a credible, substantial and specific use for the claimed mouse and one skilled in the art

would not know how to use the claimed mouse according to the embodiments disclosed by the instant specification. Therefore, the 101 rejection is maintained.

Claims 40-43, 49, 50, 52-57 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In response to this rejection, Applicant explains that wild type phenotype is the phenotype of the control mice and it establishes the reference point that allows one to establish the mutant phenotype. Applicant further asserts that the phenotype of the mSTp1 knockout mice is described in the specification in comparison to control mice. Applicant further submits a declaration from John Burke that the transgenic mice were in fact compared with controls of identical background. As such, Applicant submits that one skilled in the art would know how to make and used the claimed mouse.

The above argument has been fully considered and deemed unpersuasive. The reasons for non-enablement of the claimed invention were discussed in detail in the previous office actions. With regard to Applicant's argument of predictability of phenotype, although Applicant use gender, age and strain matched wild type controls, the phenotype of a mutant mouse is not only the result of the targeted gene, but it also reflects interactions with background genes, and other unknown mutations in the genetic background (see Crawley, pages 107 last paragraph through page 108 1st paragraph). The examiner does not doubt the statements made in the specification, but simply indicate that the specification does not provide sufficient teaching to

enable one skilled in the art to make and use the claimed invention without undue experimentation.

The examiner appreciates Applicant's clarification of "wild type phenotype." However, the examiner wish to clarify the "transgene independent phenotype" discussed in the previous office actions is not same as so called "wild type phenotype." It is referring to a phenotype exhibited by the transgenic mouse only (not the wild type mouse) but not directly result from the transgene. The specification thus needs to provide sufficient teaching so that one skilled in the art would recognize that the claimed phenotype is directly result from the gene disruption.

In response to Applicant's argument with regard to the requirement of reciting a phenotype, Applicant is reminded that according to the statue of 112 1st paragraph, critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The phenotype of the claimed mouse is critical or essential to for using the knockout mouse; therefore, need to be recited in the claim. The examiner does not agree that the phenotype is an inherent property of the claimed mouse because the phenotype of the mouse is unpredictable for reasons discussed in the previous office action and above. One skilled in the art would not know how to use the knockout mouse without any phenotype. The claims need to recite the phenotype, wherein describe them in the specification is not sufficient for enablement of the instant claimed invention.

For reasons discussed in the previous office action and above, the claimed invention is not enabled by the instant specification. Therefore, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
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